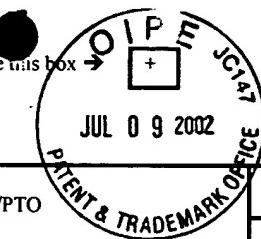


Please type a plus sign (+) inside this box



JUL 09 2002

PTO/SB/08A (08-00)

**Substitute for form 1449A/PTO**

## **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1

of 6

---

6

*Complete if Known*

<b>Application Number</b>	10/004,118
<b>Filing Date</b>	October 30, 2001
<b>First Named Inventor</b>	Moran
<b>Group Art Unit</b>	1644
<b>Examiner Name</b>	
<b>Attorney Docket Number</b>	RMED 004/011US

RECEIVED  
JUL 15 2002  
TECH CENTER 1600  
PTO/SB/08A (08-00)

U.S. PATENT DOCUMENTS

## **FOREIGN PATENT DOCUMENTS**

Examiner Signature		Date Considered	6-11-03
-----------------------	---	--------------------	---------

**\*EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number.

<sup>2</sup> See attached Kinds of U.S. Patent Documents.

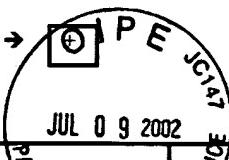
<sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

**4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.**

**5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.**

<sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Please type a plus sign (+) inside this box →



PTO/SB/08A (08-00)

Substitute for form 1449A/PTO				Complete if Known		RECEIVED JUL 13 2002 U.S. PATENT AND TRADEMARK OFFICE
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>				Application Number	10/004,118	
Sheet	2	of	6	Filing Date	October 30, 2001	
				First Named Inventor	Moran	
				Group Art Unit	1644	
				Examiner Name		
				Attorney Docket Number	BMED-004/01US	

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS				RECEIVED JUL 13 2002 U.S. PATENT AND TRADEMARK OFFICE	
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
	D1	ADOLF GR et al., Human interferon ω1: isolation of the gene, expression in Chinese hamster ovary cells and characterization of the recombinant protein. Biochimica et Biophysica Acta 1991;1089:167-174			
	D2	ADOLF GR et al., Purification and characterization of natural human interferon ω1. J. Biol. Chem. 1990;265:9290-5			
	D3	ADOLF GR., Antigenic structure of human interferon ω1 (Interferon αII1): comparison with other human interferons, J. Gen. Virol. 1987;68:1669-1676			
	D4	ADOLF GR., Monoclonal antibodies and enzyme immunoassays specific for human interferon (IFN) ω1: evidence that IFN-ω1 is a component of human leukocyte IFN, Virology 1990;175:410-71			
	D5	AULITZKY WE, Acute hematologic effects of interferon alpha, interferon gamma, tumor necrosis factor alpha and Interleukin 2, Ann. Hematol. 1991; 62: 25-31.		T <sup>2</sup>	
	D6	BALKWILL FR, Interferons. In: Cytokines in cancer therapy, Oxford University Press, 1989.			
	D7	BALKWILL, FR, Interferons, Lancet 1989; 13: 1060-1063.			
	D8	BEKKERING FC, et al., Estimation of Early Hepatitis C Viral Clearance in Patients Receiving Daily Interferon and Ribavirin Therapy Using a Mathematical Model, Hepatology 2001;33:419-23			
	D9	BOLINGER AM et al., Recombinant interferon gamma for treatment of chronic granulomatous disease and other disorders, Clin Pharm 1992 Oct;11(10):834-50			
	D10	BONKOVSKY HL et al., Outcomes research in chronic viral hepatitis C: effects of interferon therapy, In Process Citation Can J Gastroenterol 2000 Jul-Aug;14 Suppl B:21B-29B			
	D11	BORDEN EC et al., Second-generation interferons for cancer: clinical targets In Process Citation, Semin Cancer Biol 2000 Apr; 10(2):125-44			
	D12	CONDINO-NETO A; Interferon-gamma improves splicing efficiency of CYBB gene transcripts in an interferonresponsive variant of chronic granulomatous disease due to a splice site consensus region mutation, Newburger PE Blood 2000 Jun 1;95(11):3548-54			

RECEIVED

	D13	DAVIS G, et al., Durability of viral response to interferon alone or in combination with oral ribavirin in patients with chronic hepatitis C. Program and abstracts of the 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases; November 5-9, 1999; Dallas, Texas. Abstract 570.	JUL 09 2002 TECHNIER 1600/2900
	D14	DI MARCO V, et al., Combined treatment of relapse of chronic hepatitis C with high-dose alpha-2B interferon plus ribavirin for 6 or 12 months. Program and abstracts of the 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases; November 5-9, 1999; Dallas, Texas. Abstract 569.	JUL 13 2002 TECHNIER 1600/2900
	D15	ELIAS L et al., Infusional interleukin-2 and 5-fluorouracil with subcutaneous interferon-alpha for the treatment of patients with advanced renal cell carcinoma: a southwest oncology group Phase II study. Cancer 2000 Aug 1;89(3):597-603	
	D16	FANG JW S, et al., The impact of baseline liver histology on virologic response to interferon alpha-2b± rho ribavirin therapy in patients with chronic hepatitis C. Program and abstracts of the 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases; November 5-9, 1999; Dallas, Texas. Abstract 572.	
	D17	FERENCI P, et al., Combination of interferon (IFN) induction therapy and ribavirin in chronic hepatitis C. Program and abstracts of Digestive Disease Week 2000; May 21-24, 2000; San Diego, California. Abstract 977.	
	D18	FONTAINE H et al.; Recovery from chronic hepatitis C in long-term responders to ribavirin plus interferon alfa letter Pol S: Lancet 2000 Jul 1;356(9223):41	
	D19	GLUE P, et al., A dose-ranging study of Peg-intron and ribavirin in chronic hepatitis C – safety, efficacy, and virological rationale. Program and abstracts of the 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases; November 5-9, 1999; Dallas, Texas. Abstract 571.	
	D20	GONZALES HJ, et al., Randomized controlled trial including an initial 4-week “induction” period during one year of high-dose interferon alfa-2B treatment for chronic hepatitis C. Program and abstracts of Digestive Disease Week 2000; May 21-24, 2000; San Diego, California. Abstract 975.	
	D21	GRANT PR et al., Combination therapy with interferon-alpha plus N-acetyl cysteine for chronic hepatitis C: a placebo controlled double-blind multicentre study. J Med Virol 2000 Aug;61(4):439-42	
	D22	HEIM MH, Intracellular signaling and antiviral effects of interferons. Dig Liver Dis 2000 Apr;32(3):257-63	
	D23	HELLSTRAND K et al., Histamine and the response to IFN-alpha in chronic hepatitis C. Interferon Cytokine Res 1998 Jan; 18(1):21-2	
	D24	HELLSTRAND K et al., Histamine and cytokine therapy Acta Oncol 1998;37(4):347-53	
	D25	HELLSTRAND K et al., Histamine in immunotherapy of advanced melanoma: a pilot study. Cancer Immunol Immunother 1994 Dec. 39(6):416-9	
	D26	ISAACS A, et al., Virus interference. I. The interferon. Pro. R. Soc. Lond. B. Biol. Sci. 1957; 147: 258-267	

RECEIVED  
JUL 15 2002

	D27	KHALILI M et al., Interferon and ribavirin versus interferon and amantadine in interferon nonresponders with chronic hepatitis C see comments Am J Gastroenterol 2000 May;95(5):1284-9	
	D28	KITA Y et al., Characterization of a polyethylene glycol conjugate of recombinant human interferon-gamma. Drug Des Deliv 1990 Sep;6(3):157-67	TECH
O I P E JUL 15 2002	D29	KNOBLER RL et al., Systemic alpha-interferon therapy of multiple sclerosis. Neurology 1984; 34: 1273-1279	INTER JUL 15 2002
O I P E JUL 15 2002	D30	KOVACEVIC Z et al., Treatment of chronic viral hepatitis B in secondary membranoproliferative glomerulonephritis using recombinant alfa-2 interferon Maksic Dj Vojnosanit Pregl 2000 Mar-Apr;57(2):235-40	APR 2000
O I P E JUL 09 2002	D31	KRACKE A, et al., Mx proteins in blood leukocytes for monitoring interferon beta-1b therapy in patients with MS. Neurology 2000;54:193-9	
PATENT & TRADEMARK OFFICE	D32	KRONENBERGER B, et al., Influence if interferon-alpha on CD82-expression in HCV-positive patients. Program and abstracts of Digestive Disease Week 2000; May 21-24, 2000; San Diego, California. Abstract 976.	
	D33	KROWN SE; Interferons and interferon inducers in cancer treatment. Seminars in Oncology 13(2): 207-217, 1986.	
	D34	KUNZI MS, et al., Role of interferon-stimulated gene ISG-15 in the interferon-omega-mediated inhibition of human immunodeficiency virus replication. J Interferon Cytokine Res 1996;16:919-27	
	D35	LEE JH, et al., Dynamics of hepatitis C virus quasispecies turnover during interferon-A treatment. Program and abstracts of Digestive Disease Week 2000; May 21-24, 2000; San Diego, California. Abstract 974.	
	D36	LUKASZEWSKI RA et al., Pegylated alpha interferon is an effective treatment for virulent Venezuelan equine encephalitis virus and has profound effects on the host immune response to infection. J Virol 2000 Jun;74(11):5006-15	
	D37	MCHUTCHISON JG, et al., Interferon alfa-2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C. N Engl J Med. 1998;339:1485-1492.	
	D38	MERAD M et al., Generation of monocyte-derived dendritic cells from patients with renal cell cancer: modulation of their functional properties after therapy with biological response modifiers (IFN-alpha plus IL-2 and IL-12). J Immunother 2000 May-Jun;23(3):369-78	
	D39	MILELLA M, et al., Neutralizing antibodies to recombinant alpha-interferon and response to therapy in chronic hepatitis C infection. Liver 1993; 13 (3):146-150	
	D40	NEUMANN A, et al., Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon-alpha therapy. Science 282;1998:103-7	
	D41	NIEFORTH KA et al., Use of an indirect pharmacodynamic stimulation model of MX protein induction to compare in vivo activity of interferon alfa-2a and a polyethylene glycol-modified derivative in healthy subjects. Clin Pharmacol Ther 1996 Jun;59(6):63646	
	D42	OLASO V et al., Early prediction of lack of response to treatment with interferon and interferon plus ribavirin using biochemical and virological criteria in patients with chronic hepatitis C ; Esp Quimoter; 1999 Sep;12(3):220-8	

	D43	PANITCH HS, Interferons in multiple sclerosis. Drugs 1992; 44 (6): 946-962	
	D44	PIMSTONE NR, et al., High dose (780 MIU/52 weeks) interferon monotherapy is highly effective treatment for hepatitis C. Program and abstracts of Digestive Disease Week 2000; May 21-24, 2000; San Diego, California. Abstract 973.	TECH CENTER JUL 15 2002
O I P E JUL 09 2002 PATENT & TRADEMARK OFFICE	D45	POYNARD T, et al., Is an "a la carte" combined interferon alfa 2b plus ribavirin possible for the first line treatment in patients with chronic hepatitis C. Hepatology 2000;31:211-218.	1600/2900
	D46	POYNARD T, et al., Randomized trial of interferon alfa 2b plus ribavirin for 48 weeks or for 24 weeks versus interferon alfa 2b plus placebo for 48 weeks for the treatment of chronic infection with hepatitis C virus. Lancet. 1998;352:1426-1432.	
	D47	QUESADA JR et al., INTERFERONS IN HEMATOLOGICAL MALIGNANCIES: Non-serial; The Interferon System. A Current Review to 1987. Baron S et al, eds. The University of Texas Medical Branch Series in Biomedical Science, Austin, TX, University of Texas Press, p. 487-95, 1987	
	D48	SEN GC et al., The interferon system. J. Biol. Chem. 1992; 267: 5017-5020.	
	D49	SHIFFMAN ML, et al.; A decline in HCV-RNA level during interferon or interferon/ribavirin therapy in patients with virologic nonresponse is associated with an improvement in hepatic histology. Program and abstracts of the 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases; November 5-9, 1999; Dallas, Texas. Abstract 567.	
	D50	SHIMA T et al., Serum total bile acid level as a sensitive indicator of hepatic histological improvement in chronic hepatitis C patients responding to interferon treatment. J. Gastroenterol Hepatol 2000 Mar; 15(3):294-9	
	D51	SIMON JH et al., A longitudinal study of T1 hypointense lesions in relapsing MS: MSCRG trial of interferon betala. Multiple Sclerosis Collaborative Research Group. : Munschauer FE 3rd Neurology 2000 Jul 25;55(2):185-92	
	D52	SULKOWSKI M. et al., Peginterferon- $\alpha$ -2a (40kD) and ribavirin in patients with chronic hepatitis C: a phase II open label study. Biodrugs 2002;16(2):105-109	
	D53	TANAKA H et al., Effect of interferon therapy on the incidence of hepatocellular carcinoma and mortality of patients with chronic hepatitis C: a retrospective cohort study of 738 patients. Int J Cancer 2000 Sep 1;87(5):741-9	
	D54	THE IFNB MULTIPLE SCLEROSIS STUDY GROUP; Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. Neurology 1993; 43: 655-667	
	D55	TONG MJ et al., Prediction of response during interferon alfa 2b therapy in chronic hepatitis C patients using viral and biochemical characteristics: a comparison. Hepatology 1997; 26 (6):1640-1645	
	D56	TOUZA REY F et al., The clinical response to interferon-gamma in a patient with chronic granulomatous disease and brain abscesses due to Aspergillus fumigatus An Med Interna 2000 Feb; 17(2):86-7	
	D57	WEINSTOCK-GUTTMAN B et al., What is new in the treatment of multiple sclerosis? ; Drugs 2000 Mar;59(3):401-10	

	D58	WEISSMANN C, et al., The interferon genes. Prog. Nucleic Acid Res. 1986; 33: 251-300	
	D59	WRIGHT HI et al., Preliminary experience with alpha-2b-interferon therapy of viral hepatitis in liver allograft recipients. Transplantation 1992 Jan;53(1):121-4	
	D60	YOUNOSSI ZM et al., The roles of amantadine, rimantadine, ursodeoxycholic acid, and NSAIDs, alone or in combination with alpha interferons, in the treatment of chronic hepatitis C Semin Liver Dis 1999;19 Suppl 1:95-102	
JUL 09 2002	D61	ZEIN NN, Interferons in the management of viral hepatitis. Cytokines Cell Mol Ther 1998 Dec;4(4):229-41	JUL 15 2002
PATENTS & TRADEMARKS U.S. PATENT AND TRADEMARK OFFICE	D62	ZEUZEM S, et al., Hepatitis C Virus Dynamics In Vivo: Effect of Ribavirin and Interferon Alfa on Viral Turnover. Hepatology 1998;28:245-52.	TECH CENTER 1600/2000
	D63	ZIESCHE R et al., A Preliminary Study of Long-Term Treatment with Interferon Gamma-1b and Low-Dose Prednisolone in Patients with Idopathic Pulmonary Fibrosis New Engl J Med 1999; 341:1264-9.	

Examiner  
Signature

Date  
Considered

6. 11. 03

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number.

<sup>2</sup> Applicant is to place a check mark here if English language Translation attached.

Please type a plus sign (+) inside this box →

PTO/SB/08A (08-00)



Substitute for form 1449A/PTO <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)				<i>Complete if Known</i>	
Sheet	1	of	1	Application Number	10/004,118
				Filing Date	October 30, 2001
				First Named Inventor	Moran
				Group Art Unit	1644
				Examiner Name	
				Attorney Docket Number	BMED-004/01US
				RECEIVED SEP 03 2002 TECH CENTER 1600/2900	

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code <sup>2</sup> (if known)		
PL	P2	4,673,405		Guittard et al.	06-16-1987
PL	P3	5,908,621		Glue et al.	06-01-1999

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T
PL	D64	ZEIDNER et al., Treatment of FeLV-induced immunodeficiency syndrome (FeLV-FAIDS) with controlled release capsular implantation of 2', 3'-dideoxycytidine, Antiviral Research, 11 (1989) 147-160			

Examiner Signature		Date Considered	6.11.03
--------------------	--	-----------------	---------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number.

<sup>2</sup> See attached Kinds of U.S. Patent Documents.

<sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.

<sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.